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SEQUENCE LISTING

<110> Broun, Pierre

<120> METHOD FOR MODIFYING A BIOSYNTHETIC
PATHWAY

<130> 514442001200/MBI0032

<140> US 09/810,836
<141> 2001-03-16

<160> 14

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<223> G993

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Leu Ser Ile Ser Thr Thr Pro Lys Pro Thr Thr Glu Lys Lys
20 25 30

ctc tct tct ccg ccg gcg acg tcg atg cgt ctc tac aga atg gga agc 146
Leu Ser Ser Pro Pro Ala Thr Ser Met Arg Leu Tyr Arg Met Gly Ser
35 40 45

ggc gga agc agc gtc gtt ttg gat tca gag aac ggc gtc gag acc gag 194
Gly Gly Ser Ser Val Val Leu Asp Ser Glu Asn Gly Val Glu Thr Glu
50 55 60

tca cgt aag ctt cct tcg tcg aaa tat aaa ggc gtt gtg cct cag cct 242
Ser Arg Lys Leu Pro Ser Ser Lys Tyr Lys Gly Val Val Pro Gln Pro
65 70 75

aac gga aga tgg gga gct cag att tac gag aag cat cag cga gtt tgg 290
Asn Gly Arg Trp Gly Ala Gln Ile Tyr Glu Lys His Gln Arg Val Trp
80 85 90 95

ctc ggt act ttc aac gag gaa gaa gct gcg tct tct tac gac atc 338
Leu Gly Thr Phe Asn Glu Glu Glu Ala Ala Ser Ser Tyr Asp Ile
100 105 110

gcc gtg agg aga ttc cgc ggc cgc gac gcc gtc act aac ttc aaa tct 386

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Gln Val Asp Gly Asn Asp Ala Glu Ser Ala Phe Leu Asp Ala His Ser			
130	135	140	
aaa gct gag atc gtg gat atg ttg agg aaa cac act tac gcc gat gag			482
Lys Ala Glu Ile Val Asp Met Leu Arg Lys His Thr Tyr Ala Asp Glu			
145	150	155	
ttt gag cag agt aga cg ^g aag ttt gtt aac ggc gac gga aaa cgc tct			530
Phe Glu Gln Ser Arg Arg Lys Phe Val Asn Gly Asp Gly Lys Arg Ser			
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ggg ttg gag acg g ^{cg} acg tac gga aac gac gct gtt ttg aga g ^{cg} cgt			578
Gly Leu Glu Thr Ala Thr Tyr Gly Asn Asp Ala Val Leu Arg Ala Arg			
180	185	190	
gag gtt ttg ttc gag aag act gtt acg ccg agc gac gtc ggg aag ctg			626
Glu Val Leu Phe Glu Lys Thr Val Thr Pro Ser Asp Val Gly Lys Leu			
195	200	205	
aac cgt tta gtg ata ccg aaa caa cac g ^{cg} gag aag cat ttt ccg tta			674
Asn Arg Leu Val Ile Pro Lys Gln His Ala Glu Lys His Phe Pro Leu			
210	215	220	
ccg g ^{cg} atg acg acg g ^{cg} atg ggg atg aat ccg tct ccg acg aaa ggc			722
Pro Ala Met Thr Thr Ala Met Gly Met Asn Pro Ser Pro Thr Lys Gly			
225	230	235	
gtt ttg att aac ttg gaa gat aga aca ggg aaa gtg tgg cgg ttc cgt			770
Val Leu Ile Asn Leu Glu Asp Arg Thr Gly Lys Val Trp Arg Phe Arg			
240	245	250	255
tac agt tac tgg aac agc agt caa agt tac gtg ttg acc aag ggc tgg			818
Tyr Ser Tyr Trp Asn Ser Ser Gln Ser Tyr Val Leu Thr Lys Gly Trp			
260	265	270	
agc cgg ttc gtt aaa gag aag aat ctt cga gcc ggt gat gtg gtt tgt			866
Ser Arg Phe Val Lys Glu Lys Asn Leu Arg Ala Gly Asp Val Val Cys			
275	280	285	
ttc gag aga tca acc gga cca gac ccg caa ttg tat atc cac tgg aaa			914
Phe Glu Arg Ser Thr Gly Pro Asp Arg Gln Leu Tyr Ile His Trp Lys			
290	295	300	
gtc cgg tct agt ccg gtt cag act gtg gtt agg cta ttc gga gtc aac			962
Val Arg Ser Ser Pro Val Gln Thr Val Val Arg Leu Phe Gly Val Asn			
305	310	315	
att ttc aat gtg agt aac gag aaa cca aac gac gtc gca gta gag tgt			1010
Ile Phe Asn Val Ser Asn Glu Lys Pro Asn Asp Val Ala Val Glu Cys			
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gtt ggc aag aag aga tct ccg gaa gat gat ttg ttt tcg tta ggg tgt			1058
Val Gly Lys Lys Arg Ser Arg Glu Asp Asp Leu Phe Ser Leu Gly Cys			

340

345

350

tcc aag aag cag gcg att atc aac atc ttg tga caaattctt tttttgggtt 1111
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 35 40 45
 Gly Ser Ser Val Val Leu Asp Ser Glu Asn Gly Val Glu Thr Glu Ser
 50 55 60
 Arg Lys Leu Pro Ser Ser Lys Tyr Lys Gly Val Val Pro Gln Pro Asn
 65 70 75 80
 Gly Arg Trp Gly Ala Gln Ile Tyr Glu Lys His Gln Arg Val Trp Leu
 85 90 95
 Gly Thr Phe Asn Glu Glu Glu Ala Ala Ser Ser Tyr Asp Ile Ala
 100 105 110
 Val Arg Arg Phe Arg Gly Arg Asp Ala Val Thr Asn Phe Lys Ser Gln
 115 120 125
 Val Asp Gly Asn Asp Ala Glu Ser Ala Phe Leu Asp Ala His Ser Lys
 130 135 140
 Ala Glu Ile Val Asp Met Leu Arg Lys His Thr Tyr Ala Asp Glu Phe
 145 150 155 160
 Glu Gln Ser Arg Arg Lys Phe Val Asn Gly Asp Gly Lys Arg Ser Gly
 165 170 175
 Leu Glu Thr Ala Thr Tyr Gly Asn Asp Ala Val Leu Arg Ala Arg Glu
 180 185 190
 Val Leu Phe Glu Lys Thr Val Thr Pro Ser Asp Val Gly Lys Leu Asn
 195 200 205
 Arg Leu Val Ile Pro Lys Gln His Ala Glu Lys His Phe Pro Leu Pro
 210 215 220
 Ala Met Thr Thr Ala Met Gly Met Asn Pro Ser Pro Thr Lys Gly Val
 225 230 235 240
 Leu Ile Asn Leu Glu Asp Arg Thr Gly Lys Val Trp Arg Phe Arg Tyr
 245 250 255
 Ser Tyr Trp Asn Ser Ser Gln Ser Tyr Val Leu Thr Lys Gly Trp Ser
 260 265 270
 Arg Phe Val Lys Glu Lys Asn Leu Arg Ala Gly Asp Val Val Cys Phe
 275 280 285
 Glu Arg Ser Thr Gly Pro Asp Arg Gln Leu Tyr Ile His Trp Lys Val
 290 295 300
 Arg Ser Ser Pro Val Gln Thr Val Val Arg Leu Phe Gly Val Asn Ile
 305 310 315 320
 Phe Asn Val Ser Asn Glu Lys Pro Asn Asp Val Ala Val Glu Cys Val

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		Met Asp
		1
ttt gac gag gag cta aat ctt tgt att acg aaa ggt aaa aat gtt gat	164	
Phe Asp Glu Glu Leu Asn Leu Cys Ile Thr Lys Gly Lys Asn Val Asp		
5	10	15
cat tct ttt gga gga gaa gct tct tcc acg tcc cca aga tct atg aag	212	
His Ser Phe Gly Gly Glu Ala Ser Ser Thr Ser Pro Arg Ser Met Lys		
20	25	30
aaa atg aag agt cct agt cgt cct aaa ccc tat ttc caa tcc tct tct	260	
Lys Met Lys Ser Pro Ser Arg Pro Lys Pro Tyr Phe Gln Ser Ser Ser		
35	40	45
		50
tct cct tat tcg tta gag gct ttc cct ttt tct ctc gat cca aca ctt	308	
Ser Pro Tyr Ser Leu Glu Ala Phe Pro Phe Ser Leu Asp Pro Thr Leu		
55	60	65
cag aat cag caa caa ctc gga tca tac gtt ccg gta ctt gag caa	356	
Gln Asn Gln Gln Gln Leu Gly Ser Tyr Val Pro Val Leu Glu Gln		
70	75	80
cga caa gac ccg aca atg caa ggc cag aag caa atg atc tcc ttt agt	404	
Arg Gln Asp Pro Thr Met Gln Gly Gln Lys Gln Met Ile Ser Phe Ser		
85	90	95
cct caa caa caa cag cag cag cag tat atg gcc cag tac tgg agt	452	
Pro Gln Gln Gln Gln Gln Gln Tyr Met Ala Gln Tyr Trp Ser		
100	105	110
gac aca ttg aat ctg agt cca aga gga aga atg atg atg atg agc	500	
Asp Thr Leu Asn Leu Ser Pro Arg Gly Arg Met Met Met Met Ser		
115	120	125
		130
caa gaa gct gtt caa cct tac atc gca acg aag ctg tac aga gga gtg	548	
Gln Glu Ala Val Gln Pro Tyr Ile Ala Thr Lys Leu Tyr Arg Gly Val		
135	140	145

aga caa cgt caa tgg gga aaa tgg gtc gca gag atc cgt aag cca cga	596
Arg Gln Arg Gln Trp Gly Lys Trp Val Ala Glu Ile Arg Lys Pro Arg	
150 155 160	
agc agg gca cgt ctt tgg ctt ggt acc ttt gat aca gct gaa gaa gct	644
Ser Arg Ala Arg Leu Trp Leu Gly Thr Phe Asp Thr Ala Glu Glu Ala	
165 170 175	
gcc atg gcc tac gac cgc caa gcc ttc aaa tta cga ggc cac agc gca	692
Ala Met Ala Tyr Asp Arg Gln Ala Phe Lys Leu Arg Gly His Ser Ala	
180 185 190	
aca ctg aat ttc ccg gag cat ttt gtg aat aag gaa agc gag ctg cat	740
Thr Leu Asn Phe Pro Glu His Phe Val Asn Lys Glu Ser Glu Leu His	
195 200 205 210	
gat tca aac tcg tcg gat cag aaa gaa cct gaa acg cca cag cca agc	788
Asp Ser Asn Ser Ser Asp Gln Lys Glu Pro Glu Thr Pro Gln Pro Ser	
215 220 225	
gag gtt aac ttg gag agc aag gaa cta ccg gtg att gat gtt ggg aga	836
Glu Val Asn Leu Glu Ser Lys Glu Leu Pro Val Ile Asp Val Gly Arg	
230 235 240	
gag gaa ggt atg gct gag gca tgg tac aat gcc att aca tcg gga tgg	884
Glu Glu Gly Met Ala Glu Ala Trp Tyr Asn Ala Ile Thr Ser Gly Trp	
245 250 255	
ggt cct gaa agt cct ctt tgg gat gat ttg gat agt tct cat cag ttt	932
Gly Pro Glu Ser Pro Leu Trp Asp Asp Leu Asp Ser Ser His Gln Phe	
260 265 270	
tca tca gaa agc tca tct tct cct ctc tct tgt cct atg agg cct	980
Ser Ser Glu Ser Ser Ser Pro Leu Ser Cys Pro Met Arg Pro	
275 280 285 290	
ttc ttt tga aaaagtttat aaacccacat tgtgtttag gttatagttt	1029
Phe Phe *	
agggttatgc tcattggcat ttggatggag gcaattttg tcatctccca ttccaccaca	1089
tatcagtcat tatatgtgtc tacctttct ctgtatttct atcattatca ttgtttttat	1149
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aaaaaaaaaaaa aaaaaaaaaa	1226
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Val Asp His Ser Phe Gly Gly Glu Ala Ser Ser Thr Ser Pro Arg Ser	
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Met Lys Lys Met Lys Ser Pro Ser Arg Pro Lys Pro Tyr Phe Gln Ser	

35	40	45	
Ser Ser Ser Pro Tyr Ser	Leu Glu Ala Phe Pro Phe	Ser Leu Asp Pro	
50	55	60	
Thr Leu Gln Asn Gln Gln Gln Leu Gly Ser	Tyr Val Pro Val Leu		
65	70	75	80
Glu Gln Arg Gln Asp Pro Thr Met Gln Gly Gln Lys Gln Met Ile Ser			
85	90	95	
Phe Ser Pro Gln Gln Gln Gln Gln Gln Gln Tyr Met Ala Gln Tyr			
100	105	110	
Trp Ser Asp Thr Leu Asn Leu Ser Pro Arg Gly Arg	Met Met Met Met		
115	120	125	
Met Ser Gln Glu Ala Val Gln Pro Tyr Ile Ala Thr Lys Leu Tyr Arg			
130	135	140	
Gly Val Arg Gln Arg Gln Trp Gly Lys Trp Val Ala Glu Ile Arg Lys			
145	150	155	160
Pro Arg Ser Arg Ala Arg Leu Trp Leu Gly Thr Phe Asp Thr Ala Glu			
165	170	175	
Glu Ala Ala Met Ala Tyr Asp Arg Gln Ala Phe Lys Leu Arg Gly His			
180	185	190	
Ser Ala Thr Leu Asn Phe Pro Glu His Phe Val Asn Lys Glu Ser Glu			
195	200	205	
Leu His Asp Ser Asn Ser Ser Asp Gln Lys Glu Pro Glu Thr Pro Gln			
210	215	220	
Pro Ser Glu Val Asn Leu Glu Ser Lys Glu Leu Pro Val Ile Asp Val			
225	230	235	240
Gly Arg Glu Glu Gly Met Ala Glu Ala Trp Tyr Asn Ala Ile Thr Ser			
245	250	255	
Gly Trp Gly Pro Glu Ser Pro Leu Trp Asp Asp Leu Asp Ser Ser His			
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Gln Phe Ser Ser Glu Ser Ser Ser Ser Pro Leu Ser Cys Pro Met			
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Met Glu Arg Asp Asp Cys Arg Arg			
1	5		
ttt cag gac tcg ccg gcg cag acg acg gag aga aga gtg aaa tat aaa			160
Phe Gln Asp Ser Pro Ala Gln Thr Thr Glu Arg Arg Val Lys Tyr Lys			
10	15	20	
cca aag aag aaa aga gcc aaa gat gat gat gag aaa gtt gtt tcg			208
Pro Lys Lys Lys Arg Ala Lys Asp Asp Asp Glu Lys Val Val Ser			
25	30	35	40

aag cat cca aat ttt cga ggt gtc aga atg aga caa tgg gga aaa tgg Lys His Pro Asn Phe Arg Gly Val Arg Met Arg Gln Trp Gly Lys Trp	45	50	55	256
gtg tcc gaa atc aga gag cca aaa aag aaa tca aga atc tgg ctc ggt Val Ser Glu Ile Arg Glu Pro Lys Lys Ser Arg Ile Trp Leu Gly	60	65	70	304
act ttc tcc acg gcg gag atg gcg gcg cgt gct cac gac gtg gca gct Thr Phe Ser Thr Ala Glu Met Ala Ala Arg Ala His Asp Val Ala Ala	75	80	85	352
tta gcc atc aaa ggc ggt tct gca cat ctc aac ttc ccg gag ctc gct Leu Ala Ile Lys Gly Ser Ala His Leu Asn Phe Pro Glu Leu Ala	90	95	100	400
tat cac ctc cct aga cca gct agt gcc gac cct aaa gac atc caa gct Tyr His Leu Pro Arg Pro Ala Ser Ala Asp Pro Lys Asp Ile Gln Ala	105	110	115	448
120				
gcc gcc gcc gca gct gca gcc gct gtg gcc att gac atg gat gta gag Ala Ala Ala Ala Ala Ala Val Ala Ile Asp Met Asp Val Glu	125	130	135	496
acg tct tcg ccg tcg cca tct ccc aca gtt acg gaa acg tca tct ccg Thr Ser Ser Pro Ser Pro Thr Val Thr Glu Thr Ser Ser Pro	140	145	150	544
150				
gct atg ata gca ctc tcc gac gac gcg ttc tcc gat ctt cct gat ctc Ala Met Ile Ala Leu Ser Asp Asp Ala Phe Ser Asp Leu Pro Asp Leu	155	160	165	592
165				
ttg ctc aac gtg aac cat aac atc gat ggc ttc tgg gac tct ttt ccc Leu Leu Asn Val Asn His Asn Ile Asp Gly Phe Trp Asp Ser Phe Pro	170	175	180	640
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tat gaa gaa ccc ttc ctc tct caa agt tac tag aaactcaaaa ctatgtcggt Tyr Glu Glu Pro Phe Leu Ser Gln Ser Tyr *	185	190		693
190				
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Asp Asp Asp Glu Lys Val Val Ser Lys His Pro Asn Phe Arg Gly Val	35	40	45	

Arg Met Arg Gln Trp Gly Lys Trp Val Ser Glu Ile Arg Glu Pro Lys
 50 55 60
 Lys Lys Ser Arg Ile Trp Leu Gly Thr Phe Ser Thr Ala Glu Met Ala
 65 70 75 80
 Ala Arg Ala His Asp Val Ala Ala Leu Ala Ile Lys Gly Gly Ser Ala
 85 90 95
 His Leu Asn Phe Pro Glu Leu Ala Tyr His Leu Pro Arg Pro Ala Ser
 100 105 110
 Ala Asp Pro Lys Asp Ile Gln Ala Ala Ala Ala Ala Ala Ala Ala
 115 120 125
 Val Ala Ile Asp Met Asp Val Glu Thr Ser Ser Pro Ser Pro Ser Pro
 130 135 140
 Thr Val Thr Glu Thr Ser Ser Pro Ala Met Ile Ala Leu Ser Asp Asp
 145 150 155 160
 Ala Phe Ser Asp Leu Pro Asp Leu Leu Leu Asn Val Asn His Asn Ile
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 180 185 190
 Ser Tyr

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Met Val Lys Gln Ala Met Lys Glu Glu Lys Lys Arg Asn Thr Ala				
1 5 10 15				
atg cag tca aag tac aaa gga gtg agg aag agg aaa tgg gga aaa tgg				154
Met Gln Ser Lys Tyr Lys Gly Val Arg Lys Arg Lys Trp Gly Lys Trp				
20 25 30				
gta tcg gag atc aga ctt cca cac agc aga gaa cga att tgg tta ggc				202
Val Ser Glu Ile Arg Leu Pro His Ser Arg Glu Arg Ile Trp Leu Gly				
35 40 45				
tct tac gac act ccc gag aag gcg gcg cgt gct ttc gac gcc gct caa				250
Ser Tyr Asp Thr Pro Glu Lys Ala Ala Arg Ala Phe Asp Ala Ala Gln				
50 55 60				
ttt tgt ctc cgc ggc gat gct aat ttc aat ttc cct aat aat cca				298
Phe Cys Leu Arg Gly Gly Asp Ala Asn Phe Asn Phe Pro Asn Asn Pro				
65 70 75 80				
ccg tcg atc tcc gta gaa aag tcg ttg acg cct ccg gag att cag gaa				346
Pro Ser Ile Ser Val Glu Lys Ser Leu Thr Pro Pro Glu Ile Gln Glu				
85 90 95				

gct gct gct aga ttc gct aac aca ttc caa gac att gtc aag gga gaa Ala Ala Ala Arg Phe Ala Asn Thr Phe Gln Asp Ile Val Lys Gly Glu 100 105 110	394
gaa gaa tcg ggt tta gta ccc gga tcc gag atc cga cca gag tct cct Glu Glu Ser Gly Leu Val Pro Gly Ser Glu Ile Arg Pro Glu Ser Pro 115 120 125	442
tct aca tct gca tct gtt gct aca tcg acg gtg gat tat gat ttt tcg Ser Thr Ser Ala Ser Val Ala Thr Ser Thr Val Asp Tyr Asp Phe Ser 130 135 140	490
ttt ttg gat ttg ctt ccg atg aat ttc ggg ttt gat tcc ttc tcc gac Phe Leu Asp Leu Leu Pro Met Asn Phe Gly Phe Asp Ser Phe Ser Asp 145 150 155 160	538
gac ttc tct ggc ttc tcc ggt ggt gat cga ttt aca gag att tta ccc Asp Phe Ser Gly Phe Ser Gly Gly Asp Arg Phe Thr Glu Ile Leu Pro 165 170 175	586
atc gaa gat tac gga gga gag agt tta tta gat gaa tct ttg att ctt Ile Glu Asp Tyr Gly Gly Glu Ser Leu Leu Asp Glu Ser Leu Ile Leu 180 185 190	634
tgg gat ttt tga attcccaaac ataatatttt ttttagaggca actgtgagat Trp Asp Phe * 195	686
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Val Ser Glu Ile Arg Leu Pro His Ser Arg Glu Arg Ile Trp Leu Gly 35 40 45	
Ser Tyr Asp Thr Pro Glu Lys Ala Ala Arg Ala Phe Asp Ala Ala Gln 50 55 60	
Phe Cys Leu Arg Gly Gly Asp Ala Asn Phe Asn Phe Pro Asn Asn Pro 65 70 75 80	
Pro Ser Ile Ser Val Glu Lys Ser Leu Thr Pro Pro Glu Ile Gln Glu 85 90 95	
Ala Ala Ala Arg Phe Ala Asn Thr Phe Gln Asp Ile Val Lys Gly Glu 100 105 110	
Glu Glu Ser Gly Leu Val Pro Gly Ser Glu Ile Arg Pro Glu Ser Pro 115 120 125	
Ser Thr Ser Ala Ser Val Ala Thr Ser Thr Val Asp Tyr Asp Phe Ser 130 135 140	

Phe Leu Asp Leu Leu Pro Met Asn Phe Gly Phe Asp Ser Phe Ser Asp
145 150 155 160
Asp Phe Ser Gly Phe Ser Gly Gly Asp Arg Phe Thr Glu Ile Leu Pro
165 170 175
Ile Glu Asp Tyr Gly Gly Ser Leu Leu Asp Glu Ser Leu Ile Leu
180 185 190
Trp Asp Phe
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